

Comparative dissolution tests for Moxifloxacin HCl form A and form B (US20070072895) and moxifloxacin HCl US 5,849,752

Preparation of the samples

Three samples of moxifloxacin HCl were prepared:

sample 168 was made following example 2 of US20070072895 (form A),

sample 176 was made according to example 7 of US20070072895 (form B),

sample 172 was prepared to generate the monohydrate described in US 5,849,752, according to the following procedure:

In a 250 ml flask equipped with reflux condenser and mechanical stirring, 10 g of moxifloxacin HCl are introduced, followed by 100 mL of deionised water. The mixture is heated up to $70 \div 75^{\circ}\text{C}$, and dissolution of the solid is observed. The temperature is then lowered and at $50 \div 55^{\circ}\text{C}$ crystallization is observed. The mixture is brought to room temperature, maintained in these conditions for 30', filtered and washed with 10 mL of water. The wet solid is then dried under vacuum at 40°C to obtain 6,0 g of moxifloxacin HCl monohydrate.

PXRD of samples 168, 176 and 172 were first recorded to confirm identity of the different crystalline forms. The relative PXRD are reported respectively in attachment 1, attachment 2 and attachment 3.

Comparative solubility test

A comparative solubility test in water was carried out on the three materials, as follows:

Solubility of sample 168 Form A (example 2 of US20070072895)

1.6 g of sample 168 were put in a 100 mL glass becker equipped with magnetical stirring, and 15 mL of deionised water were added at room temperature. The mixture was stirred for 2 minutes, obtaining a slurry. Then several portions of deionised water were added and after each addition the mixture was stirred for 2 minutes and the aspect of the mixture was recorded. The results are reported in the following table



mL of deionised water added	Aspect of the mixture
6	slurry
10	slurry
10	slurry
10	slurry
10	slurry
10	Clear solution

Total ml of water added 71
Solubility found 22.5 mg/ml

Solubility of sample 176 Form B (example 7 of US20070072895)

1.5 g of sample 176 were put in a 100 mL glass becker equipped with magnetical stirring, and 15 mL of deionised water were added at room temperature. The mixture was stirred for 2 minutes, obtaining a slurry. Then several portions of deionised water were added and after each addition the mixture was stirred for 2 minutes and the aspect of the mixture was recorded. The results are reported in the following table

mL of deionised water added	Aspect of the mixture
10	slurry
10	slurry
10	slurry
10	slurry
10	slurry
2	Clear solution

Total ml of water added 67
Solubility found 22.4 mg/ml

Solubility of sample 172 (US 5,849,752)

1.5 g of sample 172 were put in a 100 mL glass becker equipped with magnetical stirring, and 15 mL of deionised water were added at room temperature. The mixture was stirred for 2 minutes, obtaining a slurry.

Then several portions of deionised water were added and after each addition the mixture was stirred for 2 minutes and the aspect of the mixture was recorded. The results are reported in the following table

mL of deionised water added	Aspect of the mixture
10	slurry
10	slurry
10	slurry
10	slurry
10	slurry
10	slurry
5	slurry
5	slurry
8	Clear solution

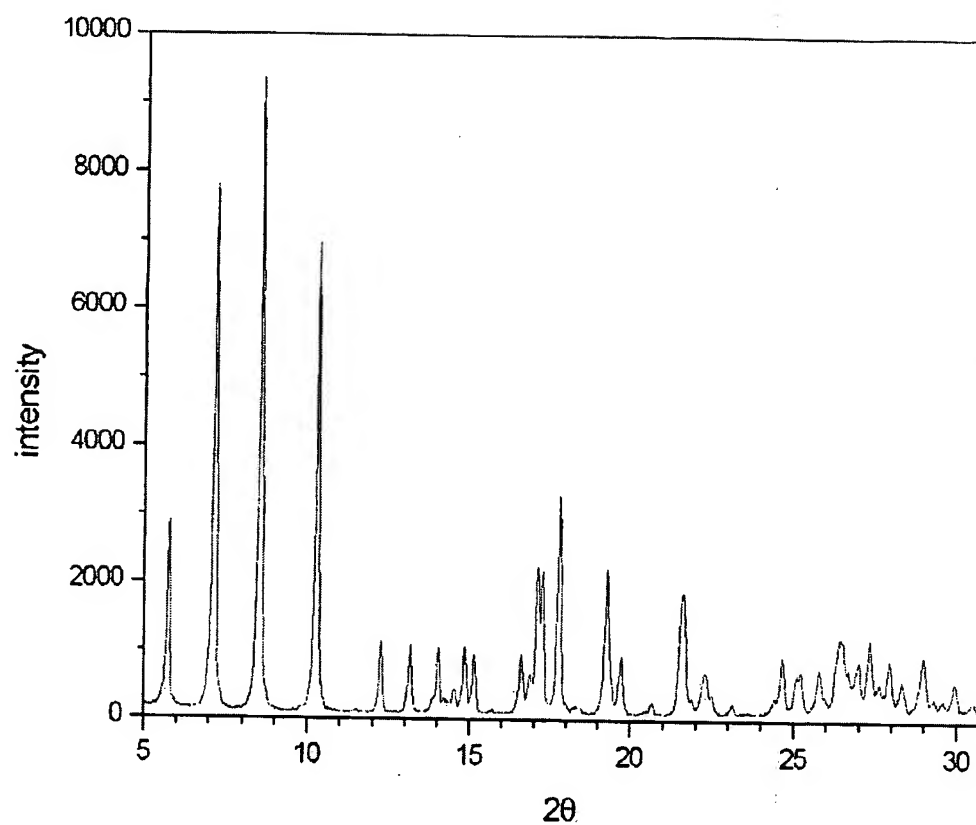
Total ml of water added 93
Solubility found 16.1 mg/ml

Conclusions

The reported experimental data, demonstrate that sample 168 and sample 167, prepared according the procedure described in US20070072895, are significantly more soluble than sample 172 prepared according to prior art teaching (US 5,849,752).

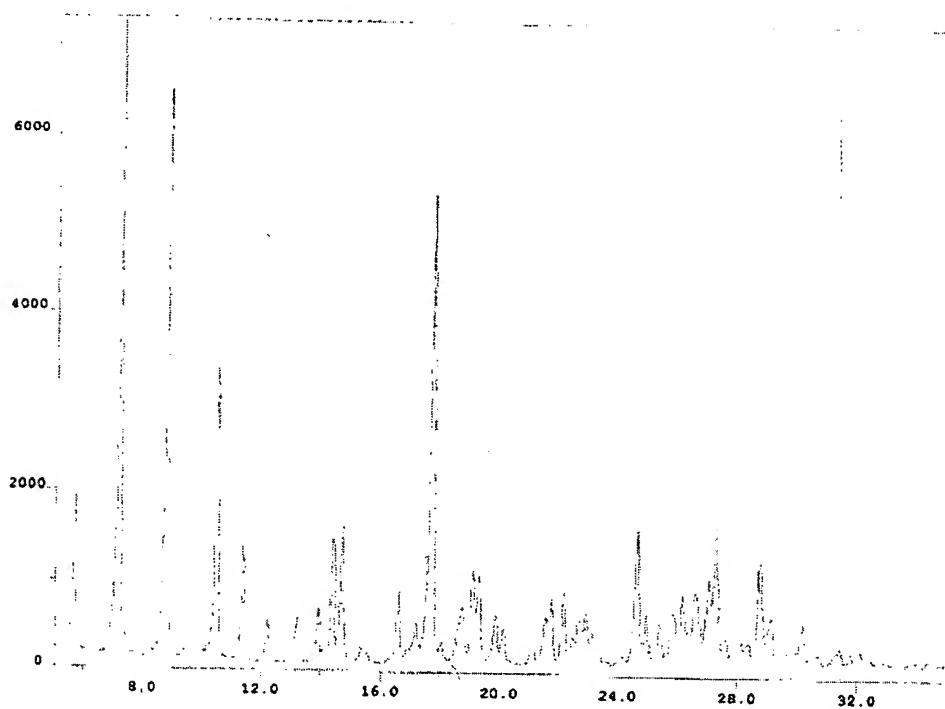
ATTACHMENT 1

PXRD of sample 168



ATTACHMENT 2

PXRD of sample 176



ATTACHMENT 3

PXRD of sample 172

